Title
Deep tissue monitoring enabled by wearable ultrasonic devices and machine learning

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Publication Date
2019

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA SAN DIEGO

Deep tissue monitoring enabled by wearable ultrasonic devices and machine learning

A Thesis submitted in partial satisfaction of the requirements for the degree

Master of Science

in

Chemical Engineering

by

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Committee in charge:

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2019

The thesis of Zhuorui Zhang is approved, and it is acceptable in quality and form for publication on microfilm and electronically:

Chair

University of California San Diego

2019

Table of Contents

List of Figures

ACKNOWLEDGEMENTS

I would like to convey my sincere and deep gratitude to my advisor Prof. Sheng Xu. During the past two years studying in the group, I had a chance to learn everything as a researcher from him, especially his strong willing and philosophy of conducting pioneer and high-quality research work, which will last long during my academic career.

I would also like to acknowledge my colleagues, Chonghe Wang, Muyang Lin, Xinyu Tian, Baiyan Qi, and everybody in the lab, without whom my research work would not be possible. They are my true comrades.

Many thanks to my parents and friends. It is your unwavering support helped me get through all the tough periods.

This paper, in full, is currently being prepared for submission for publication of the material. Zhang, Zhuorui. The dissertation/thesis author was the primary investigator and author of this material.

ABSTRACT OF THE THESIS

Deep tissue monitoring enabled by wearable ultrasonic devices and machine learning

by

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Master of Science in Chemical Engineering

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Professor Sheng Xu, Chair

Benefiting from the development of wearable electronic devices, various physiological signals, such as body temperature, hydration, glucose/lactate levels, and local field potentials, can already be monitored continuously and noninvasively. Among all physiological signals, those deeply beneath the skin, including central blood pressure, blood flow and activities of major organs, are particularly important since they are directly related to the subject's life-sustaining capability. However, there is a lack of devices that could give continuous and reliable readings of these vital signs. Their common limitations can be summarized as: limited penetration depth and operator dependence. Herein, we use human carotid artery as an example and demonstrate wearable ultrasonic devices supported by control electronics and adaptive algorithms to achieve automatic

deep tissue monitoring. To eliminate the operator dependence of ultrasound technology, machine learning-based algorithms were developed addressing the blood vessel positioning and wall tracking tasks.

Introduction

Deep tissue signals, including central blood pressure (BP) is of great importance for the general patients. Including the systolic and diastolic BP levels, BP waveforms from the deeply embedded central vessels, have been proved to contain abundant information about the cardiovascular status and can provide remarkable insights for cardiovascular disease (CVD) diagnosis and prognosis[1]. Thus, a ubiquitous monitoring device with the accessibility of BP waveforms at central spots is critically needed, especially for CVD patients who can improve their awareness of the disease and life quality. Current widely adopted devices for BP measurement can be summarized as on the basis of four methods: sphygmonanometry, arterial catheterization, photoplethysmography, and the arterial applanation tonometry. However, they all suffer from significant technical challenges preventing them from achieving continuous central BP monitoring[2-8].

Ultrasound-based technologies have the potential to overcome all of these challenges above due to the non-invasive, highly directional, and powerful tissue penetrating nature of ultrasound[9]. Benefiting from the marriage with stretchable electronics, a conformal, ultrasonic BP waveform monitoring device has been demonstrated[1]. BP waveforms at various measurement spots including the carotid artery can be obtained with high fidelity using this device. However, the reported device still faces several challenges to realize ubiquitous and convenient monitoring in clinics. To translate the ultrasound radiofrequency (RF) signals to BP waveforms, post-processing conducted by experienced operators is necessary since the translation process requires the operator to recognize the positions of pulsating blood vessel walls. This dependence on human-involved signal processing procedures precludes the device from being accessible by the general patients, which represents a major problem for locations where well-trained operators are not readily available.

In this study, we developed a device to provide a ubiquitous solution for continuous BP monitoring at central vessels. The machine learning-based algorithms were developed to address the dependence on human operators realizing blood vessel searching and signal processing in a real-time and automatic manner.

Chapter 1

1.1 Limitations of currently adopted devices for BP monitoring

Current widely adopted devices for BP measurement can be summarized as on the basis of four methods: sphygmonanometry, arterial catheterization, photoplethysmography, and the arterial applanation tonometry (Fig. 1.1). However, they all suffer from significant technical challenges preventing them from achieving continuous central BP monitoring. The sphygmomanometer is the most widely used device in clinics for BP measurement (Fig. 1.1a). An experienced doctor is required to apply an inflatable cuff on the subject's forearm and determine the BP level according to the Korotkoff sound heard during the measurement[2]. Although more advanced cuff-based devices with automatic BP estimation functions or even in ambulatory working manners are already commercially available[3-4], their common mechanism of collapsing and releasing the target artery predetermined that they are not applicable for continuous monitoring. Arterial catheterization (Fig. 1.1b, also known as cannulation) is the most accurate method for central BP monitoring, but it is too invasive to allow frequent measurements. Complications including bleeding, possible infection and risk of embolism are inevitable during its process[5]. Photoplethysmography is also frequently used for BP waveform monitoring (Fig. 1.1c). However, it cannot penetrate deep enough (< 8 mm) into the tissue to measure BP at the central spots[6], e.g., the carotid artery (~ 3 cm depth). Besides, the obtained results from photoplethysmography are not consistently accurate due to their susceptibility to heat, moisture[7] and adjacent complex vasculatures[8]. Tonometry (Fig. 1.1d) is the current noninvasive gold-standard technique to access BP waveforms at various spots. Since a pen-like device should be stably hold at the correct spot by the operator, it is highly operator-dependent, creating significant challenges for accurate and reliable measurements on arteries that are deep underneath the skin. Tiny offset from the central arterial axis or moderate holding forces of the tonometry probe will introduce tremendous recording error of the BP waveform[1].

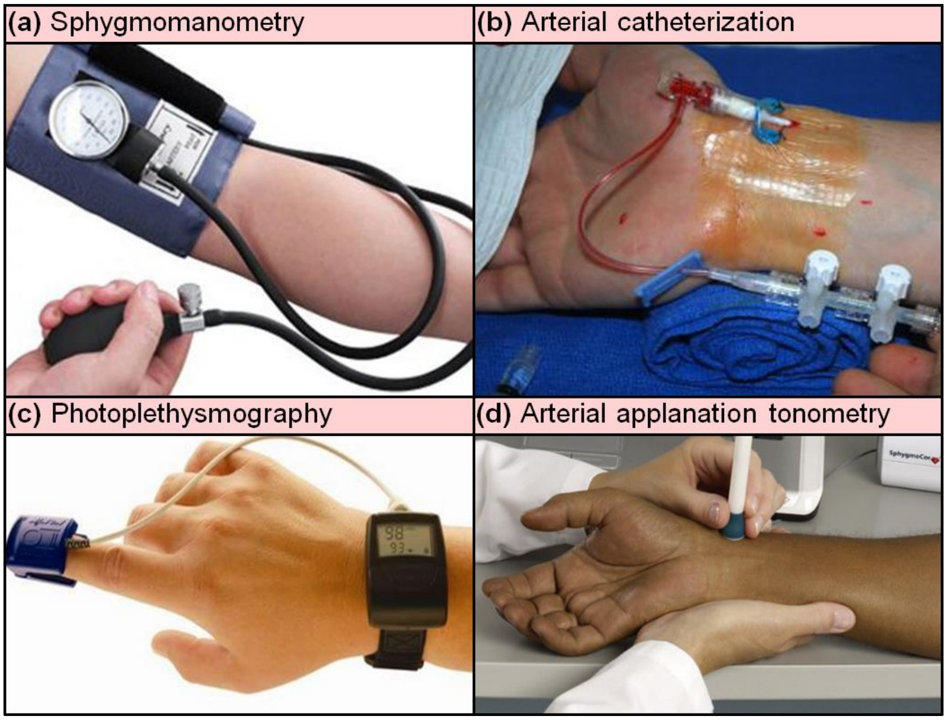

Figure 1.1: Limitations of different conventional BP sensing approaches. (a) Sphygmonanometry requires a cuff to obstruct the artery while sensing. (b) The arterial catheterization gives the most accurate reading of BP but causes bleeding and risks of infection and embolism. (c) Photoplethysmography is confined to sensing BP at very peripheral spots due to the limited light penetration depth. (d) The arterial applanation tonometry needs a well-trained operator to hold the pen-like device stably and well aligned with the arterial line.

1.2 Project innovation

Wearable devices with mechanical properties similar to the skin offer the capability of non-invasive, continuous monitoring of a variety of vital signs[10], such as local field potentials[11], temperature[12], sweat content[13], and skin hydration[14]. Our previous work demonstrated a wearable device that serves as a powerful tool for continuous BP waveform monitoring of deeply embedded vessels[1]. Base on this technique, this study further addressed the remaining challenges.

Different from only capturing signals on the skin/device interface or accessing information of shallow tissues, this research is a pioneer study to develop an operator-free monitoring system to capture medical data deeply underneath the skin. This capability is stemming from the advantages of ultrasound inspections including biocompatibility, non-invasion, and deep penetration in human tissues. However, conventional rigid ultrasonic components require frequent changes in the evaluation locations and orientations, which makes the technique highly operator dependent. Stretchable ultrasonic devices will adapt to the elastic, dynamic, and highly curvilinear surface of the human body[15-16], allowing them to maintain intimate contact at the device-skin interface, thus eliminates artifacts and operator dependency. Besides, automatic signal processing enabled by specially tailored machine learning algorithms to realize blood vessel positioning, wall recognition and tracking has never been realized in the field. Marrying wearable sensors with machine learning algorithms will establish a new paradigm to conquer the difficulty of mining useful information from huge amount of data generated by the device during continuous monitoring. This methodology will be disseminated to related communities and can have a catalytic impact on future research directions in wearable monitoring systems.

Overall, this work addressed a critical technological need for ubiquitous and continuous central BP monitoring and can have a direct impact on the current clinical and preventive care practices. The availability of a comfortable, non-invasive BP monitoring device can shift the public perception of the concept of the BP (from ‘discrete’ to ‘continuous’, and from ‘peripheral’ to ‘central’), and raise patient awareness, which may translate into significant reduction in associated mortality and healthcare costs.

Chapter 2

2.1 Blood vessel positioning via deep learning

In this chapter, we will discuss the algorithms designed for automatic vessel searching and signal processing to meet the practical need in clinics. The entire algorithm workflow is divided into two parts: vessel searching and waveform decoding. A convolutional neuron network (CNN) model will be developed to estimate if the received ultrasonic signals are from the target blood vessel and to provide feedbacks to the hardware. After the target blood vessel is properly insonated, the vessel walls will be recognized and tracked to derive the distention waveforms. BP waveforms will be translated from blood vessel distensions via established models[1].

Before decoding the BP waveforms from the ultrasound RF signals, proper insonation of the target artery should be achieved first. M-mode images, which contain the motion information of a certain ultrasound scan-line/channel, can serve as criteria of insonation estimation since they are distinctive under different insonation situations (Fig. 2.1 left). Those M-mode images of certain scan-lines across the target artery show clear vessel wall distention patterns while those of scan-lines/channels away from the target blood vessel contain no such patterns. Thus, correct configurations to achieve proper insonation can be found by analyzing and classifying their corresponding M-mode images.

Deep learning, a sub-field of machine learning, has shown substantial improvements in image classification tasks[17]. A "deep" CNN, a neural network with many layers, serves as the basic architecture to realize the classification functionality[17]. In this study, M-mode images with pre-labeled insonation situations will be input into the CNN for training. The M-mode images were collected with the commercial device and their labels were obtained from observations by an experienced operator. We collected ~13,000 M-mode images of carotid arteries from 8 subjects as the data set for model training and validation. The data set was divided to training, validation and test sets with the proportion of 7:2:4.

The transfer learning[17] strategy was be applied to accelerate the process instead of training from scratch. Deep CNNs pre-trained on large datasets (e.g., ImageNet) will be used as a starting point of the training. These CNNs have already been trained to conduct classification on thousands of object categories with millions of images, and thus, have strong potential to 'transfer their knowledge' to other image classification problems[17].

In this work, we chose the VGG-16 as a base model with pretrained weights from ImageNet. The top fully-connect layer was modified to give binary classification with sigmoid activation function. The loss function used was category-entropy. In the transfer learning process, the weights of the top-3 convolutional layers were unlocked for fine-tuning. The whole training process was conducted by Keras with the TensorFlow backend. After 50 epochs, the model's performances on both training and validation sets saturated with accuracies approaching to 1. Weights corresponding to the highest accuracy model was selected to be characterized and use.

Receiver operation characteristic (ROC) curves were used to characterize the model performances. ROCs from 6 different data sets including training and validation sets were summarized in Fig. 2.1 right. All ROCs show good performance with area under curve (AUC) over 0.9 and very low standard deviation. This result reveals the generalization capability of the model.

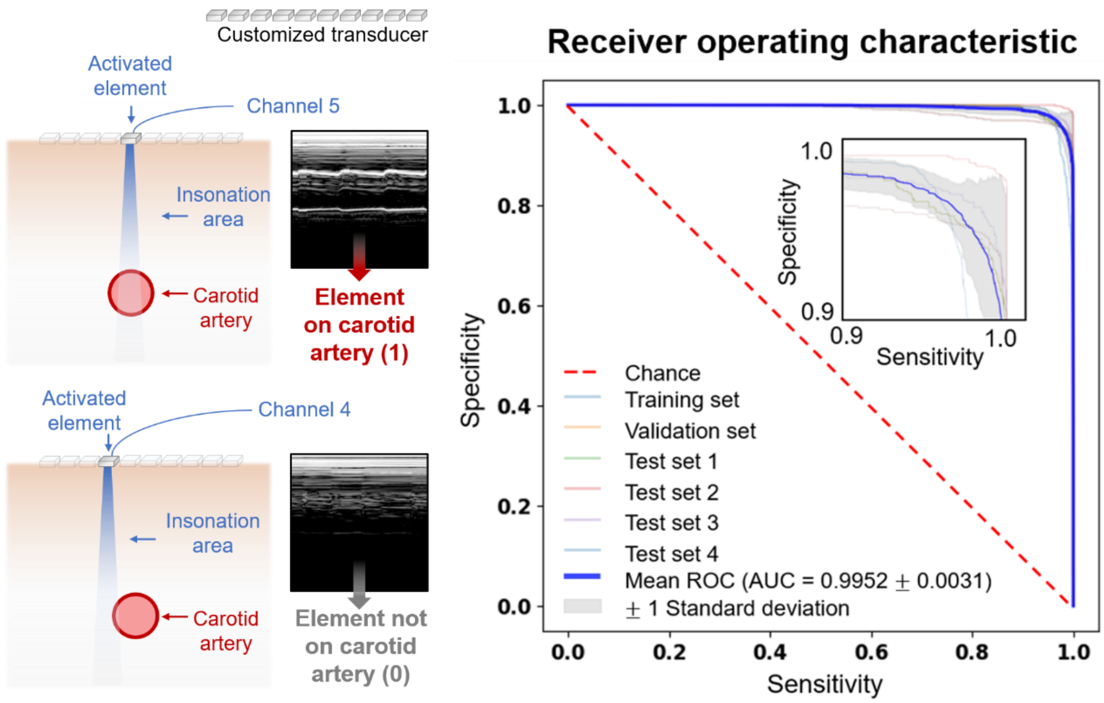

Figure 2.1: Schematics and performance of the CNN model. Schematics of different insonation circumstances and their corresponding M-mode images (left) and the ROC curve of the model (right).

2.2 Kalman filter and K-means clustering for blood vessel wall recognition and tracking

Several types of ultrasound wall tracking algorithms have been developed for decoding the blood vessel wall motions, including the auto-correlation method and the cross-correlation method[18]. In our previous work, we decoded the BP waveforms via tracking the peak shift of the ant-wall and post-wall[1]. However, all these algorithms require the operator to manually recognize peaks representing blood vessel walls in the ultrasound RF signal beforehand. In this study, we developed algorithms to automatically recognize and track these peaks based on the Kalman filter and machine learning algorithms for clustering.

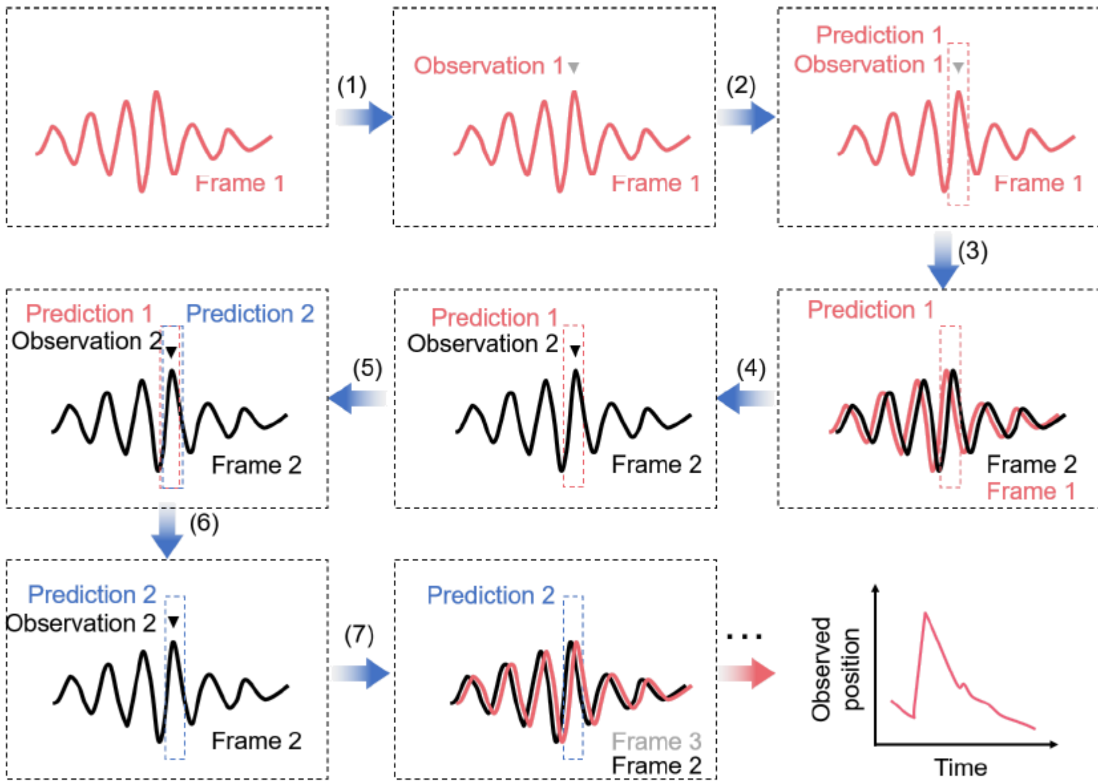

Figure 2.2: Illustration schematics of the designed Kalman filter for peak shift tracking of ultrasound RF signals. The procedure includes the following steps: (1) find a local maximum in the signal (observation); (2) apply a window to indicate range of the possible occurrence position in the next frame of signal (prediction); (3-4) find the position of the corresponding maximum in the predicted window range; (5-6) update the window range according to the new maximum position. Through this strategy, the movement trajectory of a specific maximum point will be derived, which can be translate to BP waveforms.

The Kalman filter[19] has been regarded as one of the powerful tools to solve many object tracking tasks[20]. It tracks the motion of a target object by iteratively observe and predict its displacement. In our case, the local maxima in RF signals were extracted as the 'objects' for the Kalman filter to track (Fig. 2.2). The position of a local maximum points were observed in each frame of ultrasound RF signal. Based on this observation, a range of possible positions of the same local maximum point in the next frame can be predicted. After another observation is made, the predicted positions can be updated according to the new observation. By successively conduct the aforementioned process, a trajectory of an identified maximum point can be obtained indicating its behavior over time. Using the same method to reveal movement behavior of each and every local maximum, K-means clustering[21] was applied to recognize the peaks corresponds to blood vessel walls in the ultrasound RF signals. Peak positions and their movement behavior served as the key features to identify signal segments indicating blood vessel walls. During clustering, the whole process was divided to 2 steps. The first step differentiated the initial pulses, which are stationary peaks, with pulsating blood vessel walls, which are dynamic. The total shift range during a cardiac cycle was used as the feature for clustering with k, the number of clusters, equaling two. After that, the second step was used to distinguish the anterior wall and the posterior wall according to their feature of maximum shifting velocity. During the upstroke part in a cardiac cycle, the anterior wall shifts to the left (time of flight decrease) and posterior wall shifts to the right (time of flight increase). Peaks corresponding to these two walls will have shifting speed with opposite signs. Thus, they can be fitted to two clusters and recognized.

As a preliminary test, a soft-ultrasonic device was fabricated and connected with a data acquisition and processing system based on the Verasonics hardware. The device contains two channels, one was positioned above the subject's common carotid artery and the other one was positioned away. The channel of data acquisition could be switched by software. During a 200 second test, the M-mode image of the current channel was conveyed to the CNN model every 3 second for prediction (shown in Figure 2.3 left), which corresponds to the length of screen refreshing buffer. The test begins with channel 1 and was not switched until 81s. CNN prediction results of this period ranges from 0.5697 to 0.9971 with good conformity. At the 81st second, the data acquisition channel was switched to channel 0 and the prediction result dramatically dropped to near zero. From 82 to 145s, the prediction results range from 0.0124 to 0.0895. At 146th second, the channel was switched back to 1 and the predictions also dramatically recover approaching 1. This result clearly showed the capability of the machine learning model serving as a tool for carotid artery positioning.

The performances of carotid wall tracking were also evaluated comparing with conventional wall tracking methods based on cross-correlation and auto-correlation algorithms (shown in Fig 2.3 right). The carotid artery diameter waveforms generated by this work conform to the result from cross-correlation, which is the gold standard in the field. Auto-correlation has been reported to be a effective toll for wall tracking but with inherent errors, so that its corresponding waveforms had some discrepancies.

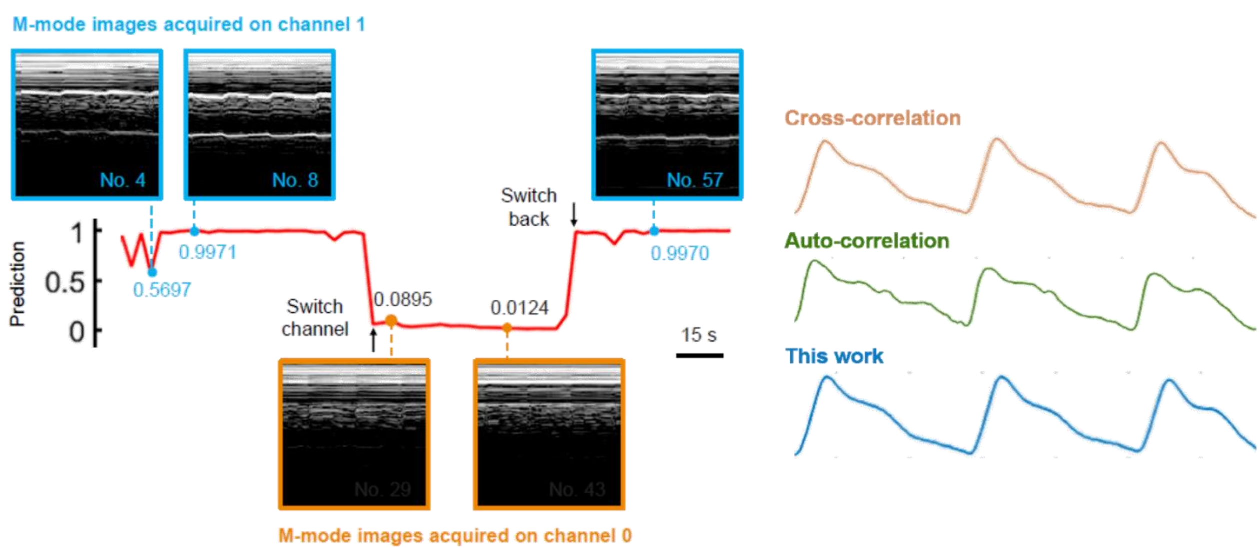

Figure 2.3: Preliminary results on image classification and wall tracking. Online prediction of a two-channel device, the channel was switched at the time points indicated by the arrows (left); Wall tracking results comparison with those processed by cross-correlation and auto-correlation methods (right).

This paper, in full, is currently being prepared for submission for publication of the material. Zhang, Zhuorui. The dissertation/thesis author was the primary investigator and author of this material.

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